

## PATENT COOPERATION TREATY

## PCT

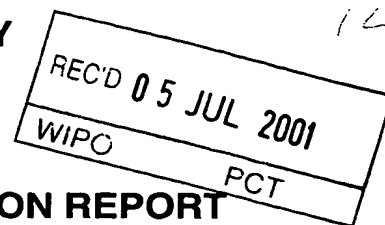
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SEP 04 2001

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

TECH CENTER 1600/2900

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference P1548R1	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/05746	International filing date (day/month/year) 02/03/2000	Priority date (day/month/year) 05/03/1999
International Patent Classification (IPC) or national classification and IPC C12N15/12		
Applicant GENENTECH, INC. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 7 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☒ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 28/09/2000	Date of completion of this report 02.07.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Bassias, I Telephone No. +49 89 2399 8106 

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/05746

## I. Basis of this report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, pages:**

1-50 as originally filed

**Claims, No.:**

1-37 as originally filed

**Drawings, sheets:**

1/11-11/11 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/05746

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

## II. Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

☐ copy of the earlier application whose priority has been claimed.

☐ translation of the earlier application whose priority has been claimed.

2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:  
**see separate sheet**

## III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 31-35.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/05746

could be formed.

☒ no international search report has been established for the said claims Nos. 31-35.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

### 1. Statement

Novelty (N)	Yes:	Claims	1-9, 11-30, 36, 37
	No:	Claims	10
Inventive step (IS)	Yes:	Claims	-
	No:	Claims	1-30, 36, 37
Industrial applicability (IA)	Yes:	Claims	1-30, 36, 37
	No:	Claims	-

2. Citations and explanations  
**see separate sheet**

## VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/US00/05746

**R Item II**

1. It appears that the priority is validly claimed. Consequently, the documents cited in the International Search Report as "P/X"-documents are not considered prior art.

**Re Item III**

1. No International Search Report was established for claims 31-35. Consequently, said claims are not subject of the present International Preliminary Examination Report (Rule 66.1(e) PCT).

**Re Item V**

1. Reference is made to the following documents (document D3 was **not** cited in the International Search Report):

D1: DELATTRE M. ET AL.: 'The Suppressor of fused gene, involved in Hedgehog signal transduction in *Drosophila*, is conserved in mammals' DEV. GENES EVOL., vol. 209, May 1999 (1999-05), pages 294-300, XP000929438

D3: DATABASE GENBANK, , GENBANK no. AA223637, 16. January 1997

2. The present application relates to the human suppressor of fused (hSu(fu)). Document D1 which is categorised in the International Search Report as a "P/X"-document and therefore not considered prior art (see Item II) refers to the suppressor of fused gene of *Drosophila melanogaster* and mentions *inter alia* a human EST having the Genbank accession number **AA223637** (D3). The sequence in D3 shows, according to "Blast", 93% identity to the sequence of the present application indicated as SEQ ID NO: 1.  
From the title of said genbank entry it can be derived that the sequence shown is similar to the mRNA sequence of the suppressor of fused gene.

Claim 10 relates to an isolated nucleic acid molecule having at least 100

nucleotides and produced by hybridizing a test molecule under stringent conditions with (a) a DNA molecule encoding a hSu(fu) polypeptide having the sequence of amino acid residues from 1 to 433 (SEQ ID NO:2), or (b) the complement of the DNA molecule of (a), and, if the test DNA molecule has at least about an 80% sequence identity to (a) or (b), isolating the test DNA.

The nucleic acid molecule of D3 falls within the scope of claim 10 since it has at least 100 nucleotides and could be produced by the method described, because it would hybridize under stringent conditions to the DNA of interest and would be isolated due to the 93% identity to the DNA of interest. Consequently, claim 10 lacks novelty over D3 (Article 33(2) PCT).

See furthermore, Item VIII, paragraph 6.

3. Having the information of document D3, a skilled person can take the clone described in D3 (the clone is available royalty-free) and can use it as a probe in order to isolate the suppressor of fused gene of human. Additionally, oligonucleotide primers could be derived from the sequence shown in D3 which could be used to find the gene claimed in the present application. Consequently, the subject-matter of claims 1-3 does not require an inventive activity (Article 33(3) PCT).
4. All the following claims (4-30, 36 and 37) are obvious products or methods which directly or indirectly relate to the subject-matter of claim 1 and for which no inventive activity is required. Hence, said claims (4-30, 36 and 37) do also not meet the requirements of Article 33(3) PCT.

#### **Re Item VIII**

1. The terms "from about" or "about" used in several claims, e.g., claims 7-10 render the scope of the respective claims unclear (Article 6 PCT). With these undefined terms also nucleic acid molecules are embraced encoding polypeptides which are smaller than the **comple** hSu(fu) polypeptide (consisting of amino acid residues **1-433**). Said molecules risk to lack novelty over sequences

disclosed in e.g., D3.

The same applies for claims using said unclear and broad terms in context of polypeptides, e.g. claims 19-22.

2. Claim 22 relating to hSu(fu) polypeptide or a **fragment** thereof is not in accordance to Article 6 PCT since a fragment merely defined by immunological features is not supported over its entire range by the description. Furthermore, said immunological features are not necessarily characterising for the peptide/fragment claimed since antibodies can bind also to sites (e.g., structures encoded by consensus sequences) which are not specific for the peptides of interest.
3. Claim 4 does not meet the requirements of Article 6 PCT since the hybridizing conditions are not defined in said claim.
4. A polypeptide "**scoring at least 80% positives**" to the sequence of a compared polypeptide (claims 9 and 21) is not clear in the sense of Article 6 PCT.
5. The expression "**control sequences**" from e.g. claim 12 lacks clarity (Article 6 PCT). A definition as given in the description (page 9, lines 14-17) could overcome said objection.
6. Claims 10 and 24 define a product by the process with which it is obtained (product-by-process). Applicant's attention is drawn to the fact that the jurisprudence of the member states is not homogenous with respect to this type of claims. Under the EPC novelty would be recognized **only** if the product itself is distinguishable from others in the prior art.

**PALM INTRANET**

Day : Thursday  
Date: 8/30/2001  
Time: 10:24:59

**Application Number Information**

Application Number :  
**09/581742 Assignments**

Filing Date : **06/16/2000**

Application Received : **06/16/2000**

Patent Number :

Issue Date : **00/00/0000**

Date of Abandonment : **00/00/0000**

Attorney Docket Number : **P1548R1**

Status : **041 / NON-FINAL ACTION MAILED**

Location : **16C1/TECH CENTER 1600-CENTRAL FILE CM-1 11C10** Location Date : **04/11/2001**

Charge to Location : /

Charge to Name : **No Charge to Name**

Station location : **FILE 1600**

Title of Invention :

**HUMAN SUPPRESSOR OF FUSED**

Examiner Number : **77076/BRANNOCK, MICHAEL**  
**T**

Group Art Unit : **1646**

Class/Subclass :  
**435/069.100**

Lost Case : **NO**

Interference Number :

Unmatched Petition : **NO**

L&R Code : **01**

Response Code : **CRF.**

Response Begin Date :  
**02/20/2001**

Response Due Date :  
**03/22/2001**

Status Date : **02/20/2001**

**Appln**  
**Info**

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PCT

## REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

Receiving Office use only

**PCT/US** 00/05746  
International Application No.

International Filing Date **02 MAR 2000**

**PCT INTERNATIONAL APPLICATION FORM**  
Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference  
(if desired) (12 characters maximum) **P1548R1**

**Box No. I TITLE OF INVENTION**  
HUMAN SUPPRESSOR OF FUSED

**Box No. II APPLICANT**

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

GENENTECH, INC.  
1 DNA Way  
South San Francisco, California 94080-4990  
US

☐ This person is also inventor.

Telephone No.  
650-225-1000

Facsimile No.  
650-952-9881

Teleprinter No.

State (that is, country) of nationality:

US

State (that is, country) of residence:

US

This person is applicant for the purposes of:



all designated States



all designated States except the United States of America



the United States of America only



the States indicated in the Supplemental Box

**Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)**

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

De SAUVAGE, Frederic J.  
187 Shooting Star Isle  
Foster City, CA 94404  
US

This person is:

☐ applicant only

☒ applicant and inventor

☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

BE

State (that is, country) of residence:

US

This person is applicant for the purposes of:



all designated States



all designated States except the United States of America



the United States of America only



the States indicated in the Supplemental Box



Further applicants and/or (further) inventors are indicated on a continuation sheet.

**Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE**

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:



agent



common representative

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

SVOBODA, Craig G.  
GENENTECH, INC.  
1 DNA Way  
South San Francisco, California 94080-4990  
US

Telephone No.

650-225-1489

Facsimile No.

650-952-9881

Teleprinter No.

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

## Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet should not be included in the request.

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

GURNEY, Austin L.  
1 Debbie Lane  
Belmont, CA 94002  
US

This person is:

- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

US

State (that is, country) of residence:

US

This person is applicant for the purposes of:

☐ all designated States☐ all designated States except the United States of America☒ the United States of America only☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

MURONE, Maximilien  
217-C Richmond Drive  
Millbrae, CA 94030  
US

This person is:

- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

CH

State (that is, country) of residence:

US

This person is applicant for the purposes of:

☐ all designated States☐ all designated States except the United States of America☒ the United States of America only☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

ROSENTHAL, Arnon  
40 Tulip Court  
Burlingame, CA 94010  
US

This person is:

- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

US

State (that is, country) of residence:

US

This person is applicant for the purposes of:

☐ all designated States☐ all designated States except the United States of America☒ the United States of America only☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

STONE, Donna M.  
684 Sierra Point Road  
Brisbane, CA 94005  
US

This person is:

- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

US

State (that is, country) of residence:

US

This person is applicant for the purposes of:

☐ all designated States☐ all designated States except the United States of America☒ the United States of America only☐ the States indicated in the Supplemental Box☒ Further applicants and/or (further) inventors are indicated on another continuation sheet.

## Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

*If none of the following sub-boxes is used, this sheet should not be included in the request.*

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

WOOD, William I.  
35 Southdown Court  
Hillsborough, CA 94010  
US

This person is:

- ☐ applicant only  
☒ applicant and inventor  
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

US

State (that is, country) of residence:

US

This person is applicant for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only  
☐ applicant and inventor  
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

State (that is, country) of residence:

This person is applicant for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only  
☐ applicant and inventor  
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

State (that is, country) of residence:

This person is applicant for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only  
☐ applicant and inventor  
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

State (that is, country) of residence:

This person is applicant for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on another continuation sheet.

**Box No.V DESIGNATION OF STATES**

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

**Regional Patent**

- ☒ **AP ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ **EA Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ **EP European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ **OA OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)

**National Patent** (if other kind of protection or treatment desired, specify on dotted line):

- |   |   |
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| <input checked="" type="checkbox"/> <b>BR</b> Brazil                                | <input checked="" type="checkbox"/> <b>MN</b> Mongolia                                  |
| <input checked="" type="checkbox"/> <b>BY</b> Belarus                               | <input checked="" type="checkbox"/> <b>MW</b> Malawi                                    |
| <input checked="" type="checkbox"/> <b>CA</b> Canada                                | <input checked="" type="checkbox"/> <b>MX</b> Mexico                                    |
| <input checked="" type="checkbox"/> <b>CH and LI</b> Switzerland and Liechtenstein  | <input checked="" type="checkbox"/> <b>NO</b> Norway                                    |
| <input checked="" type="checkbox"/> <b>CN</b> China                                 | <input checked="" type="checkbox"/> <b>NZ</b> New Zealand                               |
| <input checked="" type="checkbox"/> <b>CR</b> Costa Rica                            | <input checked="" type="checkbox"/> <b>PL</b> Poland                                    |
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| <input checked="" type="checkbox"/> <b>DE</b> Germany                               | <input checked="" type="checkbox"/> <b>RU</b> Russian Federation                        |
| <input checked="" type="checkbox"/> <b>DK</b> Denmark                               | <input checked="" type="checkbox"/> <b>SD</b> Sudan                                     |
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| <input checked="" type="checkbox"/> <b>EE</b> Estonia                               | <input checked="" type="checkbox"/> <b>SG</b> Singapore                                 |
| <input checked="" type="checkbox"/> <b>ES</b> Spain                                 | <input checked="" type="checkbox"/> <b>SI</b> Slovenia                                  |
| <input checked="" type="checkbox"/> <b>FI</b> Finland                               | <input checked="" type="checkbox"/> <b>SK</b> Slovakia                                  |
| <input checked="" type="checkbox"/> <b>GB</b> United Kingdom                        | <input checked="" type="checkbox"/> <b>SL</b> Sierra Leone                              |
| <input checked="" type="checkbox"/> <b>GD</b> Grenada                               | <input checked="" type="checkbox"/> <b>TJ</b> Tajikistan                                |
| <input checked="" type="checkbox"/> <b>GE</b> Georgia                               | <input checked="" type="checkbox"/> <b>TM</b> Turkmenistan                              |
| <input checked="" type="checkbox"/> <b>GH</b> Ghana                                 | <input checked="" type="checkbox"/> <b>TR</b> Turkey                                    |
| <input checked="" type="checkbox"/> <b>GM</b> Gambia                                | <input checked="" type="checkbox"/> <b>TT</b> Trinidad and Tobago                       |
| <input checked="" type="checkbox"/> <b>HR</b> Croatia                               | <input checked="" type="checkbox"/> <b>TZ</b> United Republic of Tanzania               |
| <input checked="" type="checkbox"/> <b>HU</b> Hungary                               | <input checked="" type="checkbox"/> <b>UA</b> Ukraine                                   |
| <input checked="" type="checkbox"/> <b>ID</b> Indonesia                             | <input checked="" type="checkbox"/> <b>UG</b> Uganda                                    |
| <input checked="" type="checkbox"/> <b>IL</b> Israel                                | <input checked="" type="checkbox"/> <b>US</b> United States of America                  |
| <input checked="" type="checkbox"/> <b>IN</b> India                                 | <input checked="" type="checkbox"/> <b>UZ</b> Uzbekistan                                |
| <input checked="" type="checkbox"/> <b>IS</b> Iceland                               | <input checked="" type="checkbox"/> <b>VN</b> Viet Nam                                  |
| <input checked="" type="checkbox"/> <b>JP</b> Japan                                 | <input checked="" type="checkbox"/> <b>YU</b> Yugoslavia                                |
| <input checked="" type="checkbox"/> <b>KE</b> Kenya                                 | <input checked="" type="checkbox"/> <b>ZA</b> South Africa                              |
| <input checked="" type="checkbox"/> <b>KG</b> Kyrgyzstan                            | <input checked="" type="checkbox"/> <b>ZW</b> Zimbabwe                                  |
| <input checked="" type="checkbox"/> <b>KP</b> Democratic People's Republic of Korea |   |
| <input checked="" type="checkbox"/> <b>KR</b> Republic of Korea                     |   |
| <input checked="" type="checkbox"/> <b>KZ</b> Kazakhstan                            |   |
| <input checked="" type="checkbox"/> <b>LC</b> Saint Lucia                           |   |
| <input checked="" type="checkbox"/> <b>LK</b> Sri Lanka                             |   |

Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet:

☐   
 ☐

**Precautionary Designation Statement:** In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)

**Supplemental Box** If the Supplemental Box is not used, this sheet should not be included in the request.

1. If, in any of the Boxes, the space is insufficient to furnish all the information: in such case, write "Continuation of Box No. ..." [indicate the number of the Box] and furnish the information in the same manner as required according to the captions of the Box in which the space was insufficient, in particular:

- (i) if more than two persons are involved as applicants and/or inventors and no "continuation sheet" is available: in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below;
- (ii) if, in Box No. II or in any of the sub-boxes of Box No. III, the indication "the States indicated in the Supplemental Box" is checked: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is applicant;
- (iii) if, in Box No. II or in any of the sub-boxes of Box No. III, the inventor or the inventor/applicant is not inventor for the purposes of all designated States or for the purposes of the United States of America: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the inventor(s) and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is inventor;
- (iv) if, in addition to the agent(s) indicated in Box No. IV, there are further agents: in such case, write "Continuation of Box No. IV" and indicate for each further agent the same type of information as required in Box No. IV;
- (v) if, in Box No. V, the name of any State (or OAPI) is accompanied by the indication "patent of addition," or "certificate of addition," or if, in Box No. V, the name of the United States of America is accompanied by an indication "continuation" or "continuation-in-part": in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI), the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application;
- (vi) if, in Box No. VI, there are more than three earlier applications whose priority is claimed: in such case, write "Continuation of Box No. VI" and indicate for each additional earlier application the same type of information as required in Box No. VI;
- (vii) if, in Box No. VI, the earlier application is an ARIPO application: in such case, write "Continuation of Box No. VI", specify the number of the item corresponding to that earlier application and indicate at least one country party to the Paris Convention for the Protection of Industrial Property or one Member of the World Trade Organization for which that earlier application was filed.

2. If, with regard to the precautionary designation statement contained in Box No. V, the applicant wishes to exclude any State(s) from the scope of that statement: in such case, write "Designation(s) excluded from precautionary designation statement" and indicate the name or two-letter code of each State so excluded.

3. If the applicant claims, in respect of any designated Office, the benefits of provisions of the national law concerning non-prejudicial disclosures or exceptions to lack of novelty: in such case, write "Statement concerning non-prejudicial disclosures or exceptions to lack of novelty" and furnish that statement below.

**Continuation of Box IV:**

BUTING, Walter E.  
 BARNES, Elizabeth M.  
 CONLEY, Deirdre L.  
 HASAK, Janet E.  
 JOHNSTON, Sean A.  
 KLEID, Dennis G.  
 KRESNAK, Mark T.  
 KUBINEC, Jeffrey S.  
 LEE, Wendy M.  
 LOVE, Richard B.  
 SCHWARTZ, Timothy R.  
 TAN, Lee K.

All of:

GENENTECH, INC.  
 1 DNA Way  
 South San Francisco, California 94080-4990  
 US

<b>Box No. VI PRIORITY CLAIM</b>		<input type="checkbox"/> Further priority claims are indicated in the Supplemental Box.		
Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application: country	regional application: * regional Office	international application: receiving Office
item (1) 05 March 1999 (05.03.99)	60/123,090	US		
item (2) 25 May 1999 (25.05.99)	60/135,736	US		
item (3)				

☒ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s): (1), (2)

\* Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.

### Box No. VII INTERNATIONAL SEARCHING AUTHORITY

**Choice of International Searching Authority (ISA)**  
(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):

ISA / EP

**Request to use results of earlier search; reference to that search** (if an earlier search has been carried out by or requested from the International Searching Authority):

Date (day/month/year)

Number

Country (or regional Office)

### Box No. VIII CHECK LIST; LANGUAGE OF FILING

This international application contains the following number of sheets:

request : 6

description (excluding sequence listing part) : 50

claims : 3

abstract : 1

drawings : 12

sequence listing part of description : 0

Total number of sheets : 72

This international application is accompanied by the item(s) marked below:

1. ☒ fee calculation sheet

2. ☐ separate signed power of attorney

3. ☒ copy of general power of attorney; reference number, if any:

4. ☐ statement explaining lack of signature

5. ☐ priority document(s) identified in Box No. VI as item(s):

6. ☐ translation of international application into (language):

7. ☐ separate indications concerning deposited microorganism or other biological material

8. ☐ nucleotide and/or amino acid sequence listing in computer readable form

9. ☒ other (specify): Transmittal Letter

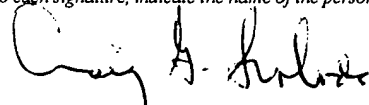
Figure of the drawings which should accompany the abstract: 1

Language of filing of the international application:

English

### Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).



Craig G. Svoboda  
Agent for Applicants

For receiving Office use only		2. Drawings:  <input type="checkbox"/> received:  <input type="checkbox"/> not received:
1. Date of actual receipt of the purported international application:	410 Rec'd PCT/PTO 05.03.00 2 MAR 2000	
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:		
4. Date of timely receipt of the required corrections under PCT Article 11(2):		
5. International Searching Authority (if two or more are competent): ISA / EF	6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid.	

For International Bureau use only

Date of receipt of the record copy by the International Bureau: